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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/639,948	08/12/2003	Rajat Sethi	12695.6USD6	6989

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EXAMINER	
JONES, DWAYNE C	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/639,948	SETHI ET AL.	
	Examiner	Art Unit	
	Dwayne C Jones	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-12 are pending.

2. Claims 1-12 are rejected.

Response to Arguments

3. Applicants' arguments filed October 6, 2004 have been fully considered but they are not persuasive. Applicants present the following issues. First, applicants purport that the term "analogue" is enabled by the instant specification. Second, applicants submit that there is no motivation to combine Smith et al. with DiPiro and no suggestion of all the claim limitations in the cited references. Third, applicants next argue that there is no suggestion in the disclosure of Smith et al. that vitamin B_6 derivatives were contemplated, especially since vitamin B_6 is not pharmaceutically equivalent to the active metabolites. Fourth, Lobel is not applicable to the instant claims.

4. First, applicants purport that the term "analogue" is enabled by the instant specification. The instant specification has not provided support the 3-acylated analogues of pyridoxal compounds such as with protein or even carbohydrate structure analogues as well as heterocyclic organic analogues.

5. Second, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Smith et al. teach that one of the causes of the microvascular events leading to ischemia in the medial temporal lobe is a moderate deficiency in vitamin B_{12} and folate, which leads to elevated homocysteine levels in the plasma, because vitamin B_{12} and folate are required cofactors in the conversion of homocysteine to methione. Homocysteine can have a toxic effect on the blood vessels that initiates the pathological cascade process leading to changes in the microvasculature, (see page 2, lines 5-12 and 31-36). Smith et al. teach of the administration angiotensin-converting enzyme (ACE) inhibitors, such as enalapril, to treat high blood pressure, (see page 3). Smith et al. also teach that the administration of ACE-inhibitors and angiotensin II antagonists are known to reduce the damage to the endothelium and to the elastic laminae in arterioles caused by homocysteine. DiPiro teach congestive heart failure can be the result of many causes, inter alia, hypertension and vasoconstriction, (see pages 115-118). DiPiro also disclose of the pathophysiology of congestive heart failure is the result of many contributing factors, namely pressure overload, volume overload, loss of muscles, decreased contractility and disturbances in filling. This decrease may further be the consequence of hypertrophy of the ventricle that may produce dramatic changes in compliance. DiPiro also disclose that hypertension, coronary artery disease, and restricted ventricular compliance may be brought about by scar formation after an infarct or even excessive hypertrophy, (see page 115). For these reasons, the skilled artisan

would have been motivated to use the teachings of Smith et al. to treat a variety of ailments that are related to occlusive vascular disease, such as the reduced blood flows in patients with various heart abnormalities that relate to congestive heart failure, namely hypertrophy.

6. Third, applicants next argue that there is no suggestion in the disclosure of Smith et al. that vitamin B_6 derivatives were contemplated, especially since vitamin B_6 is not pharmaceutically equivalent to the active metabolites. Once the compounds of the prior art reference are administered to an individual in need thereof, the vitamin B_6 compound will be metabolized by the body and the presence of these metabolites, as well as their properties, are inherent with the administration of vitamin B_6 (pryidoxine), see Shering Corporation vs. Geneva Pharmaceuticals, Inc. and Novarits Corporation and Teva Pharmaceuticals Usa, Inc. and Andrx Corporation, Andrx Pharmaceuticals, Inc. and Mylan Pharmaceuticals, Inc. and Wyeth, Esi-Lederle, Wyeth Pharmaceuticals, and Wyeth Consumer Healthcare (formerly American Home Products Corporation, Wyeth-Ayerst Laboratories, and Whitehall Robbins Healthcare) and IMPAX Laboratories, Inc. Apotex, Inc. and Novex Pharma, Copley Pharmaceutical, Inc. and GENPHARM, INC. (CAFC, 02-1540, -1541, -1542, -1543, -1544, -1545, -1546, -1547, -1548, -1549, 03-1021, -1022, -1023, -1025, -1027, 8/1/2003).

7. Fourth, Lobel is not applicable to the instant claims. Lobel teaches of pharmaceutical compositions that contain cardiovascular drugs as well as various compounds of the pyridoxine family, inter alia, pyridoxamine, pyridoxal, pyridoxal phosphate complex and pyridoxamine phosphate complex, (see column 1).

Accordingly, the skilled artisan is provided with various members of the pyridoxine family that may be used pharmaceutically to treat an individual in need thereof. Moreover, when the well known compounds of the pyridoxine family, inter alia, pyridoxamine, pyridoxal, pyridoxal phosphate complex and pyridoxamine phosphate complex (as evidenced by Lobel) are combined with the teachings of Smith et al. of WO 98/19690 in view of DiPiro the instant claims are clearly rendered obvious.

Information Disclosure Statement

8. The information disclosure statement filed on October 6, 2004 has been reviewed and considered, see enclosed copy of PTO FORM 1449.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

10. The rejection of claims 1 and 4-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the 3-acylated analogues of pyridoxal compounds of claims 2, 3, and pyridoxal-5-phosphate for the treatment of hypertrophy does not reasonably provide enablement for other types of 3-acylated analogues of pyridoxal is maintained and repeated. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

11. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed to pyridoxal-containing compositions and methods of treating hypertrophy. The method comprises administering pyridoxal-containing compositions and methods of treating hypertrophy.

(2) The state of the prior art

The compounds of the inventions are pyridoxal-containing compositions. However, the prior art does not teach that all analogues of these pyridoxal-containing compositions to various types of analogues such as carbohydrates, DNA, glycerides, heteroaryl moieties, see WO 98/19690.

(3) The relative skill of those in the art

The relative skill of those in the art of pharmaceuticals is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. Supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24 (CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5 (BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 999 F.2d 1557, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or

pharmaceutical activity of pyridoxal-containing compositions prior to filing of the instant invention was an unpredictable art.

(5) The breadth of the claims

The instant claims are very broad. For instance, claim 1 is directed to the plethora of compounds of the generic term of pyridoxal-containing compositions. The breadth of claims was a factor in Amgen v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d (Fed. Cir.),cert. Denied, 502 U.S. 856 (1991). In the Amgen case, the patent claims were directed to DNA sequences that encoded amino acid sequences. Because a very small change in the amino acid sequence of a protein can result in a very large change in the structure-function activity of a protein and because the laws of protein folding are in such a primitive state, predicting protein structure (and hence, activity) while knowing only the sequence of the protein is akin to predicting the weather for a date in the future.

(6) The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the degree of predictability in the art. In re Fisher, 839, 166 USPQ 24. Thus, although a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements, in cases involving unpredictable factors, such as most chemical reactions and physiological activity, more teaching or guidance is required. In re Fischer, 427 F.2d 839, 166 USPQ 24; Ex Parte

Hitzeman, 9 USPQ 2d 1823. For example, the Federal Circuit determined that, given the unpredictability of the physiological activity of RNA viruses, a specification requires more than a general description and a single embodiment to provide an enabling disclosure for a method of protecting an organism against RNA viruses. In re Wright, 999 F.2d 1562-63, 27 USPQ2d 1575. In the instant case, given the unpredictability of the physiological or pharmaceutical activity of a pyridoxal-containing compositions to be effective in treating hypertrophy is insufficient for enablement other than compounds of the 3-acylated analogues of pyridoxal compounds of claims 2, 3, and pyridoxal-5-phosphate The specification provides no guidance, in the way of enablement for pyridoxal-containing compositions other than the 3-acylated analogues of pyridoxal compounds of claims 2, 3, and pyridoxal-5-phosphate. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." The article "Broader than the Disclosure in Chemical Cases," 31 J.P.O.S. 5, by Samuel S. Levin covers this subject in

detail. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(7) The presence or absence of working examples

As stated above, the specification discloses pyridoxal-containing compositions that have the ability of treating hypertrophy. However, the instant specification only has enablement for analogous of pyridoxal-containing compositions of 3-acylated analogues of pyridoxal compounds of claims 2, 3, and pyridoxal-5-phosphate.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the analogues or

derivatives of pyridoxal-containing compositions that would be enabled in this specification.

Claim Rejections - 35 USC § 103

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. The rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Haque of U.S. Patent No. 6,339,085 is removed in response to the remarks and the showing under 37 CFR 1.132.

15. The rejection of claims 1-12 under 35 U.S.C. 103(a) as being unpatentable over Smith et al. of WO 98/19690 in view of DiPiro is maintained and repeated. Smith et al. teach that one of the causes of the microvascular events leading to ischemia in the medial temporal lobe is a moderate deficiency in vitamin B_{12} and folate, which leads to elevated homocysteine levels in the plasma, because vitamin B_{12} and folate are

required cofactors in the conversion of homocysteine to methione. Homocysteine can have a toxic effect on the blood vessels that initiates the pathological cascade process leading to changes in the microvasculature, (see page 2, lines 5-12 and 31-36). Smith et al. teach of the administration angiotensin-converting enzyme (ACE) inhibitors, such as enalapril, to treat high blood pressure, (see page 3). Smith et al. also teach that the administration of ACE-inhibitors and angiotensin II antagonists are known to reduce the damage to the endothelium and to the elastic laminae in arterioles caused by homocysteine. In addition, Smith et al. disclose that ACE-inhibitors are known to potentiate the response of the endothelium to agonists that increase the release of endothelium-derived relaxing factors, such as nitric oxide, (see page 4, lines 16-33). Smith et al. specifically, teach of the concurrent administration of vitamin B_6 or B_{12} in combination with an ACE inhibitor or an angiotensin II antagonist in order to modify the deleterious effects of homocysteine on the vasculature, (see page 5, lines 7-20). Smith et al. also disclose the term occlusive vascular disease encompasses inter alia, stroke and TIA, (see page 6, lines 16-19). DiPiro teach congestive heart failure can be the result of many causes, inter alia, hypertension and vasoconstriction, (see pages 115-118). DiPiro also disclose of the pathophysiology of congestive heart failure is the result of many contributing factors, namely pressure overload, volume overload, loss of muscles, decreased contractility and disturbances in filling. This decrease may further be the consequence of hypertrophy of the ventricle that may produce dramatic changes in compliance. DiPiro also disclose that hypertension, coronary artery disease, and restricted ventricular compliance may be brought about by scar formation after an infarct

or even excessive hypertrophy, (see page 115). Accordingly, the skilled artisan would have been motivated to use the teachings of Smith et al. to treat a variety of ailments that are related to occlusive vascular disease, such as the reduced blood flows in patients with various heart abnormalities that relate to congestive heart failure, namely hypertrophy. It is well known in the art that vitamin B_6 is embraced by pryidoxine and related compounds, such as pyridoxal and pyridoxamine, (see Stedman's Medical Dictionary, 25th Edition, page1726). For these reasons, it would have been obvious to one having ordinary skill in the art to employ these compositions especially since it is shown in the prior art that these compositions, namely Vitamin B_6 and its related compounds such as pyridoxamine and pyridoxal 5'-phosphate and other structurally related compounds of pyridoxine, as well as ACE inhibitors and angiotensin II antagonists are known to treat microvascular events that lead to the treatment of hypertrophy.

16. The rejection of claims 1-12 under 35 U.S.C. 103(a) as being unpatentable over Smith et al. of WO 98/19690 in view of DiPiro in view of Lobel of U.S. Patent No. 3,282,778 is maintained and repeated. Smith et al. teach that one of the causes of the microvascular events leading to ischemia in the medial temporal lobe is a moderate deficiency in vitamin B_{12} and folate, which leads to elevated homocysteine levels in the plasma, because vitamin B_{12} and folate are required cofactors in the conversion of homocysteine to methione. Homocysteine can have a toxic effect on the blood vessels that initiates the pathological cascade process leading to changes in the microvasculature, (see page 2, lines 5-12 and 31-36). Smith et al. teach of the

administration angiotensin-converting enzyme (ACE) inhibitors, such as enalapril, to treat high blood pressure, (see page 3). Smith et al. also teach that the administration of ACE-inhibitors and angiotensin II antagonists are known to reduce the damage to the endothelium and to the elastic laminae in arterioles caused by homocysteine. In addition, Smith et al. disclose that ACE-inhibitors are known to potentiate the response of the endothelium to agonists that increase the release of endothelium-derived relaxing factors, such as nitric oxide, (see page 4, lines 16-33). Smith et al. specifically, teach of the concurrent administration of vitamin B_6 or B_{12} in combination with an ACE inhibitor or an angiotensin II antagonist in order to modify the deleterious effects of homocysteine on the vasculature, (see page 5, lines 7-20). Smith et al. also disclose the term occlusive vascular disease encompasses inter alia, stroke and TIA, (see page 6, lines 16-19). DiPiro teach congestive heart failure can be the result of many causes, inter alia, hypertension and vasoconstriction, (see pages 115-118). DiPiro also disclose of the pathophysiology of congestive heart failure is the result of many contributing factors, namely pressure overload, volume overload, loss of muscles, decreased contractility and disturbances in filling. This decrease may further be the consequence of hypertrophy of the ventricle that may produce dramatic changes in compliance. DiPiro also disclose that hypertension, coronary artery disease, and restricted ventricular compliance may be brought about by scar formation after an infarct or even excessive hypertrophy, (see page 115). Accordingly, the skilled artisan would have been motivated to use the teachings of Smith et al. to treat a variety of ailments that are related to occlusive vascular disease, such as the reduced blood flows in patients with

various heart abnormalities that relate to congestive heart failure, namely hypertrophy. It is well known in the art that vitamin B_6 is embraced by pryidoxine and related compounds, such as pyridoxal and pyridoxamine, (see Stedman's Medical Dictionary, 25th Edition, page 1726). In addition, Lobel teach of pharmaceutical compositions that contain cardiovascular drugs as well as various compounds of the pyridoxine family, inter alia, pyridoxamine, pyridoxal, pyridoxal phosphate complex and pyridoxamine phosphate complex, (see column 1). Accordingly, it would have been obvious to one having ordinary skill in the art to utilize this old pharmaceutical composition for a new intended use. For these reasons, it would have been obvious to one having ordinary skill in the art to employ these compositions especially since it is shown in the prior art that these compositions, namely Vitamin B_6 and its related compounds such as pyridoxamine and pyridoxal 5'-phosphate and other structurally related compounds of pyridoxine, as well as ACE inhibitors and angiotensin II antagonists are known to treat microvascular events that lead to the treatment of hypertrophy.

Obviousness-type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. The rejection of claims 1 and 3-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 46-48 of U.S. Patent No. 6,339,085 is maintained and repeated. Once again this rejection can be obviated with the submission of a terminal disclaimer over U.S. Patent No. 6,339,085. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and U.S. Patent No. 6,339,085 teach treating hypertrophy in a mammal with the administration of the 3-acylated compounds of the formula in claim 1 concurrently with angiotensin converting enzyme inhibitor, an angiotensin II receptor antagonist, and a calcium channel blocker, a vasodilator, a diuretic, and mixtures thereof. Furthermore, the instant invention and U.S. Patent No. 6,339,085 both teach enterally or parenterally administering these compounds as well as unit dosage forms of the compound disclosed in claim 1.

18. The rejection of claims 1 and 3-12 are directed to an invention not patentably distinct from claims 1 and 46-48 of commonly assigned U.S. Patent No. 6,339,085 is withdrawn in response to the remarks of October 6, 2004.

19. The provisional rejection of claims 1, 2, and 4-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 and 40-42 of copending Application No. 09/863,093 is maintained and repeated. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant invention and copending Application No.

09/863,093 teach of treating hypertrophy with the concurrent administration of 3-acylated pyridoxal compounds of claim 1 along with additional cardiovascular compounds *inter alia*, ACE inhibitors and angiotensin II antagonists and calcium channel blockers.

20. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

21. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. C. Jones whose telephone number is (571) 272-0578. The examiner can normally be reached on Mondays, Tuesdays, Wednesdays, and Fridays from 8:30 am to 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, may be reached at (571) 272-0951. The official fax No. for correspondence is (571)-273-8300.

Also, please note that U.S. patents and U.S. patent application publications are no longer supplied with Office actions. Accordingly, the cited U.S. patents and patent application publications are available for download via the Office's PAIR, see http://pair-direct.uspto.gov. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 1-866-217-9197 (toll free).

DWAYNE JONES
PRIMARY EXAMINER
Tech. Ctr. 1614
January 10, 2005